Europäisches Patentamt | European Patent Office | Office européen des brevets

REC'D 23 JUL 2004
WIPO PCT

Bescheinigung | Certificate | Attestation

Die angehefteten Unterlagen stimmen mit der ursprünglich eingereichten Fassung der auf dem nächsten Blatt bezeichneten europäischen Patentanmeldung überein.

The attached documents are exact copies of the European patent application described on the following page, as originally filed.

Les documents fixés à cette attestation sont conformes à la version initialement déposée de la demande de brevet européen spécifiée à la page suivante.

Patentanmeldung Nr. | Patent application No. | Demande de brevet n°

03076842.8

Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets
p.o.

R C van Dijk

Anmeldung Nr:
Application no.: 03076842.8
Demande no:

Anmeldetag:
Date of filing: 13.06.03
Date de dépôt:

Anmelder/Applicant(s)/Demandeur(s):

DSM IP Assets B.V.
Het Overloon 1
6411 TE Heerlen
PAYS-BAS

Bezeichnung der Erfindung/Title of the invention/Titre de l'invention:
(Falls die Bezeichnung der Erfindung nicht angegeben ist, siehe Beschreibung.
If no title is shown please refer to the description.
Si aucun titre n'est indiqué se referer à la description.)

Encasulated materials

In Anspruch genommene Priorität(en) / Priority(ies) claimed /Priorité(s) revendiquée(s)
Staat/Tag/Aktenzeichen/State/Date/File no./Pays/Date/Numéro de dépôt:

Internationale Patentklassifikation/International Patent Classification/
Classification internationale des brevets:

B01J13/00

Am Anmeldetag benannte Vertragstaaten/Contracting states designated at date of filing/Etats contractants désignées lors du dépôt:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL
PT RO SE SI SK TR LI

ENCAPSULATED MATERIALS

The invention relates to a process for forming capsules. An encapsulation process generally comprises the following steps:

(a) forming a dispersion of a core material in a continuous phase containing a wall forming material;

(b) depositing the wall material upon the surface of a core material to form capsules;

(c) hardening of the capsules; and

(d) recovering the capsules

The continuous phase in step (a) is normally a solution of the wall material. If the core is a liquid, it is dispersed or emulsified in said solution; if, however, the core is a solid, it is usually pre-ground to the desired size and then dispersed within the solution. Step (b) generally involves changing the conditions of the solution in such a way as to cause phase separation of the wall material from the continuous phase. Normally, the wall material is caused to phase separate as a coherent liquid film around the particles or droplets of the core phase. This liquid or gelatinous wall phase is subsequently hardened (step (c)), before recovery of the capsules, if the desired product is individual capsules, i.e., a dry powder. Capsule recovery is effected by filtering, centrifuging and the like, followed by drying. In some instances, the dried product is a caked powder and must be reduced to a free flowing powder by a gentle grinding operation, e.g., sieving.

A well known and often used wall forming material is melamine-formaldehyde resin. The thus formed melamine-formaldehyde capsules are e.g. used to encapsulate aromatizing and flavoring agents and vitamins.

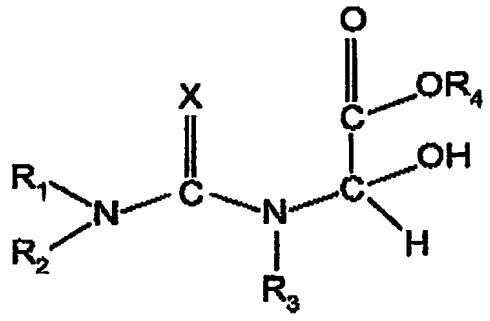
An important drawback of melamine-formaldehyde as wall forming material is that a slight formaldehyde emission is still observed. During the production of the resin and the encapsulated product, but also from the capsule itself, vapours are released that may be irritating and even toxic. Residues of the original raw materials always remain behind, also after polymerization. In cured condition, formaldehyde slowly diffuses from the product. This formaldehyde emission is not desirable, definitely not in a confined area. In such areas formaldehyde is inhaled and contacts the eyes, mouth and other parts of the body. Formaldehyde gas causes irritation of the eyes and respiratory tract and is toxic. A disadvantage of the capsules based on melamine-formaldehyde capsules therefore is the formation of the injurious free formaldehyde

An aim of the present invention is to provide a process for forming capsules, which do not release free formaldehyde. This aim is achieved in a process of (1) forming a solution of a compound (I) from an amino compound/alkanol hemiacetal mixture in a solvent,

(2) forming a dispersion of a core material in the solution,

(3) depositing the compound as a resin upon the surface of the core material to form capsules;

(4) and optionally hardening and isolating the capsules, wherein the compound (I) is a compound according to the following formula:

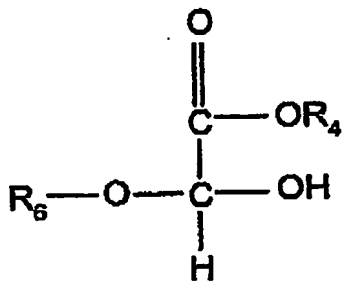


(I)

where: X is equal to O or NR_5; R_4 is equal to a H, C_1-C_{12} alkyl group, aryl group, aralkyl group or cycloalkyl group;R_1, R_2, R_3, R_5 are equal to an H, alkyl, cycloalkyl, aryl of heterocyclic group, and where R_1, R_2, and R_5 or R_1, R_2, and R_3 may together form a heterocyclic group.

Preferably R_4 is a C_1-C_{12} alkyl group. Examples hereof are methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl etc. R_4 is in particular a methyl group or an ethyl group.

The first step in the process of the invention is forming a solution of a compound according to formula (I). A compound according to formula (I) can be prepared by reacting an amino compound and an alkanol hemiacetal of the following general formula (II):



(II)

where R_4 and R_6 are a C_1-C_{12} alkyl group, aryl group, aralkyl group or cycloalkyl group, in which process an alkanol is released.

Preferably R_4 and R_6 are C_1-C_{12} alkyl groups. Examples hereof are methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl etc. R_4 and R_6 are in particular a methyl group or an ethyl group.

Examples of alkanol hemiacetals of formula II are:
methylglyoxylate methanol hemiacetal (GMHA®, DSM Fine Chemicals, Linz);
ethylglyoxylate ethanol hemiacetal (GEHA®, DSM Fine Chemicals, Linz);
ethylglyoxylate methanol hemiacetal; butylglyoxylate butanol hemiacetal;
butylglyoxylate methanol hemiacetal; butylglyoxylate ethanol hemiacetal;
isopropylglyoxylate isopropanol hemiacetal; propylglyoxylate propanol hemiacetal;
cyclohexylglyoxylate methanol hemiacetal and 2-ethylhexylglyoxylate methanol hemiacetal. It is also possible to use ethyl or butyl glyoxylate in stead of the hemiacetal.

An amino compound is defined herein as a compound having at least one NH or NH_2 group, attached to an electron-withdrawing atom or to an atom that is connected to electron-withdrawing atom or group. The number of amino groups per amino compound generally is at most 3. Examples of electron-withdrawing atoms are oxygen, nitrogen and sulphur. Suitable amino compounds are for example triazines, guanidine and mixtures of these compounds. Aminoplasts such as melamine-formaldehyde, urea-formaldehyde and melamine-urea-formaldehyde may also be employed as amino compound. Preferably, triazines such as melamine, melam, melem, ammeline, ammelide and ureidomelamine are used. In particular melamine is used.

Step (1) and (2) can be carried out in the reversed sequence or parallel, such that the solution and the dispersion both in the solvent are mixed together.

The first step in the process of the invention is forming a solution of a compound (I) from an amino compound/alkanol hemiacetal mixture in a solvent. In this

first step a wall forming material is made. The process for the preparation of the compound according to formula (I) will usually occur spontaneously once the amino compound and the alkanol hemiacetal according to formula (II) have been brought into contact with each other. The temperature in the present process can thus vary within wide limits, and preferably lies between 10°C and 90°C. Most preferably the process is carried out at between 40°C and 80°C.

The pressure in the present process preferably is between 0.005 MPa and 1.0 MPa, preferably between 0.02 MPa and 0.1 MPa. The process is preferably carried out in a solvent such as for example water or a mixture of water and alkanol. Water is the preferred solvent. Examples of alkanols are methanol, ethanol, propanol, butanol, pentanol.

Starting from the fact that the number of amino groups per amino compound generally is at most 3, the molar amino group/hemiacetal ratio preferably is between 3 and 1. The compound according formula (1) spontaneously polymerizes to a resin within the preferred temperature range of 40°C and 80°C. With more than 3 amino groups per hemiacetal, the molecular weight of the resin will be limited, while a ration below 1 is limiting for crosslinking of the resin and leaves free hemiacetal in the solvent.

The second step in the process of the invention is forming a dispersion of a core material in the solution. If the core is a first liquid, the material to be encapsulated can be this first liquid. The core material can also be a solid or a second liquid which is dissolved or dispersed in said first liquid. Said first liquid preferably is a high boiling hydrophobic liquid such as an oil. Suitable oils, are in particular partly hydrogenated terphenyls, chlorinated paraffins, alkylated biphenyls, alkyl naphthalenes, diaryl methane derivatives, dibenzyl benzene derivatives, alkanes, cycloalkanes and esters, such as phthalates, adipates, trimellitates and phosphates, and silicone oils.

To stabilize the dispersion a surfactant can be added. Suitable surfactants can be found among ionic and non-ionic surfactants. The surfactant preferably is an anionic or non-ionic surfactant. It is not always necessary to use such a surfactant, since many of the compounds according to formula (II) spontaneously form small amounts of anionic groups through hydrolysis which can act as a surfactant.

The third step in the process of the invention is depositing the compound as a resin upon the surface of the core material to form capsules. Step (3)

generally involves changing the conditions in such a way as to cause phase separation of the wall material from the continuous wall solution phase. Normally, the wall forming material is caused to phase separate as a coherent liquid film around the particles or droplets of the core phase in a process which preferably lasts between several minutes and hours. Phase separation can be introduced by an increase or decrease of the temperature. A decrease of temperature causes phase separation due to a decreased solubility, while an increase of the temperature may cause the resin to pass over its cloud point.

An alternative way of phase separation is to increase the molecular weight of the resin. This is effected by prolonged polymerization of the compound according to formula (1) in the solvent. This will decrease the solubility of the resin in the solvent.

A third way to introduce phase separation is to increase or to decrease the concentration of the resin, thus using the fact that resins from compounds according to formula (I) generally have a range of maximum solubility.

The optional forth step in the process of the invention is the hardening and isolation of the capsules. In this case the liquid or gelatinous wall phase is preferably hardened, before isolation of the capsules, if the desired product is individual capsules, i.e., a dry powder. Hardening can be done by lowering the temperature below the T_g of the resin, or by polymerisation of the resin in order to obtain an elastic non-sticky capsule. Capsule recovery can be effected by filtering, centrifuging, followed by drying or by spray drying. In some instances, the dried product is a caked powder and must be reduced to a free flowing powder by a gentle grinding operation, e.g., sieving.

The encapsulated products of the present invention also find applications due to their unique properties in the formulation of compositions for widely diversified fields of use. In the cosmetic field, products such as soap bars, fragrant in lotions and creams can be formulated containing encapsulated water soluble ingredients which would be unstable or incompatible in unencapsulated form in the presence of other ingredients of the particular formulation. For example, since certain antibacterials such as the chlorinated phenols and neomycin sulfate are incompatible on prolonged contact with soap, the present invention makes possible the formulation of a soap bar containing both of these ingredients.

In the agricultural field, encapsulated food supplements and pest control agents can be advantageously formulated. For example, water-soluble

fertilizers such as ammonium nitrate, urea and superphosphate can be encapsulated for application to the soil when a slow release or extended action is desirable, e.g., where rapid release would "burn" the vegetation. For the control of pests, encapsulated insecticides can be deposited on vegetation or in the soil without harm to the vegetation; moreover, the insecticide is not dissolved and washed away by moisture or rain, thereby allowing the insecticide to remain where deposited until ingested by the insect. Antihelminthic agents such as piperazine phosphate or citrate, and methyl rosaniline chloride when encapsulated can be incorporated into feed material for domestic animals, the encapsulated antihelminthic thereby being tasteless in the feed and also protected from decomposition during storage of the feed. Rodenticides such as calcium cyanide, thallium sulfate and sodium fluoroacetate, which are unstable in the presence of moisture or have an odor or taste repellent to the rodent are advantageously encapsulated.

Vitamins, minerals, amino acids and other food supplements, when encapsulated can be incorporated in animal feeds and be protected from decomposition during storage periods from such adverse conditions as air, moisture, and incompatible ingredients in the feed composition itself. In a similar manner, food supplements can be incorporated in compositions for human use.

The way to release the core material strongly depends on the application. Generally it is aimed that the core material is released when the capsules are consumed. Examples of consumed encapsulated materials are fragrants released during ironing or in washing machines, and flavours released from food while being eaten.

The release of the core material can be caused by different mechanisms. A first mechanism is a mechanical stress. In this way ink is released from ink comprising capsules used in copy paper. An example of the release of the core material by a temperature increase is found in flavoring additives applied in soup. Another way to release the core material is by controlled hydrolisis e.g. initiated by a decrease or increase of the pH of the aqueous environment, applied in encapsulated fragrants for (dish) washing machines or enzymatic release in drugs comprising capsules. In order to control the release speed, the thickness of the encapsulating wall can be adapted to the requirements of the specific application. A simple way to control the wall thickness is by choosing the concentration of the mixture in the solvent taking into account the particle size in relation to the wall thickness. The weight ratio of the mixture and the solvent generally is between 0.05 and 0.8, whereby the precise ranges

strongly depend on the solubility of the specific compound according to formula (I) used. Compounds according to formula (I) typically have a maximum solubility within the above mentioned range. The precise range for a particular compound can easily be established by a person skilled in the art.

The present invention also finds application in medical treatment of both animals and humans. Medicaments can be encapsulated by the method of the present invention to give a sustained release upon ingestion with resultant sustained therapeutic action. Coatings which will not dissolve in the stomach can be formulated to overcome the problem of gastric irritation or nausea caused by such medicaments as emetine hydrochloride, quinacrine hydrochloride and para-aminosallcylic acid. Similarly, medicaments such as penicillin and certain glandular extracts which are inactivated by the acid condition or enzymes encountered in the stomach are advantageously encapsulated.

The invention further relates to an encapsulated material comprising a core material, and a wall material, characterized in that the wall material comprises a resin comprising a compound according to formula (I).

The invention further relates to an encapsulated material comprising a core material, and a wall material, characterized in that the wall material comprises a resin comprising a compound according to formula (I). In a preferred encapsulated material according to the invention is the heterocyclic group formed by R_1, R_2 and R_5, an aminotriazine ring, R_3 is H and R_4 is methyl or ethyl. In a more preferred encapsulated material according to the invention is the aminotriazine ring derived from melamine.

An additional advantage of the encapsulated material according to the invention is, that hydrolyses of the wall material takes place above 85°C.

The invention is further elucidated in the following non-limiting example.

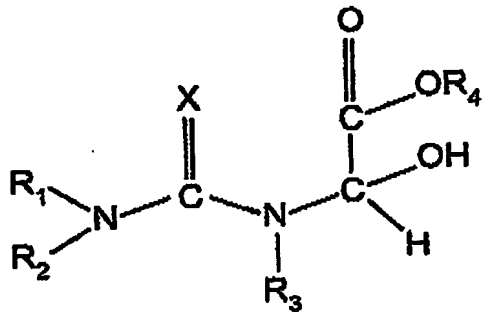
Example I

In a reaction vessel 62.9 gram melamine, 89.2 gram methyl glyoxylate and 64.8 gram water was added. This mixture was under constant stirring, heated up in a oil bad of 80°C until the melamine reacted completely with the glyoxylate and the resin is clear. Then 50 gram of paraffin oil at 80°C is, under fierce stirring with a Ultra Turrax T25 at 24,000 rpm, carefully mixed in. To stabilize the dispersion of oil and resin a surfactant (Disperbyk-181) was added. The warm oil/resin dispersion was

under stirring, added to cold water. The oil/resin dispersion precipitates in the water. The precipitated oil/resin particles were filtered with a paper filter and the particles were dried in vacuum oven at 50°C.

CLAIMS

1. Process for forming capsules comprising:
   (1) forming a solution of a compound (I) from an amino compound/alkanol hemiacetal mixture in a solvent
   (2) forming a dispersion of a core material in the solution
   (3) depositing the compound as a resin upon the surface of the core material to form capsules;
   (4) and optionally recovering the capsules, wherein the compound (I) is a compound according to the following formula:



(I)

where: X is equal or NR_5; R_4 is equal to a C_1-C_{12} alkyl group, aryl group, aralkyl group or cycloalkyl group; R_1, R_2, R_3, R_5 are equal to an H, alkyl, cycloalkyl, aryl of heterocyclic group, and where R_1, R_2, and R_5 or R_1, R_2, and R_3 may together form a heterocyclic group.

2. Process according to claim 1, wherein the solvent is water
3. Process according to claim 1, wherein the molar amino group/hemiacetal ratio is between 3 and 1.
4. Encapsulated material comprising a core material, and a wall material, characterized in that the wall material comprises a resin comprising a compound according to formula (I) of claim 1.
5. Encapsulated material according to claim 4, wherein the heterocyclic group formed by R_1,.R_2 and R_5, is an aminotriazine ring, R_3 is H and R_4 is methyl or ethyl.
6. Encapsulated material according to claim 5, wherein the aminotriazine ring is derived from melamine.

ABSTRACT

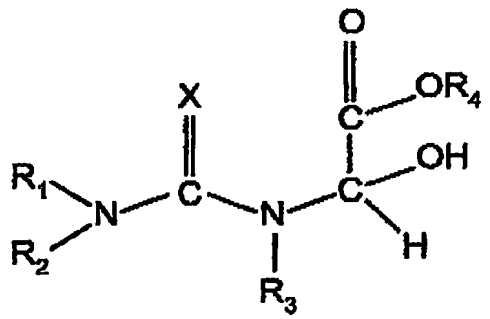
The invention relates to a process for forming capsules comprising:

(1) forming a solution of a compound (I) from an amino compound/alkanol hemiacetal mixture in a solvent

(2) forming a dispersion of a core material in the solution

(3) depositing the compound as a resin upon the surface of the core material to form capsules;

(4) and optionally recovering the capsules, wherein the compound (I) is a compound according to the following formula:



(I)

where: X is equal or NR_5; R_4 is equal to a C_1-C_{12} alkyl group, aryl group, aralkyl group or cycloalkyl group; R_1, R_2, R_3, R_5 are equal to an H, alkyl, cycloalkyl, aryl of heterocyclic group, and where R_1, R_2, and R_5 or R_1, R_2, and R_3 may together form a heterocyclic group. The invention also relates to an encapsulated material comprising a core material, and a wall material, characterized in that the wall material comprises a resin comprising a compound according to formula (I).